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EXAMINER
WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
1637	29

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/485,245	Applicant(s) Hopkins, A
	Examiner Wilder	Art Unit 1237

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *May 29, 2003* .

2a) [X] This action is **FINAL**. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1 and 3-6* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1 and 3-6* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [X] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [X] All b) [ ] Some* c) [ ] None of:

1. [X] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____ .
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [ ] Information Disclosure Statement(s) (PTO-1449) Paper No(s).
4) [ ] Interview Summary (PTO-413) Paper No(s).
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

FINAL ACTION

1. Applicant's amendment filed in Paper No. 27 is acknowledged. Claims 1, 3-6 are pending in the instant application. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follows. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims.

This Action is made FINAL.

2. The text of those sections of title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous rejections

3. The prior art rejection under 35 USC 103(a) is maintained and discussed below.

Claim Rejections - 35 USC § 103

4. Claims 1, 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Godiska et al. (5,759804, filed November 17, 1993) in view of Shen et al. (EP 0 726 310 A1 February 09, 1996). Regarding claims 1, 3 and 4, Godiska et al teach a labeling composition comprising a random mixture of oligonucleotides which are 6-mers, wherein the composition further contains at least a supply of nucleotides for chain extension, a labeled nucleotide, and a polymerase enzyme (col. 8, lines 27-31). The labeling composition of Godiska et al differs from the instant invention in that Godiska et al do not expressly teach wherein the labeling composition is in a dry state. Shen et al

teach a composition similar to that of Godiska et al present in a dry state (page 4, lines 37-41). Shen et al teach wherein the composition may comprise primers, a polymerase enzyme, a supply of nucleotides for chain extension, and a stabilizer (page 6, lines 3-7 and 22). Shen et al teach that the composition present in the dry state is advantageous because the composition is stable for a prolonged period, even when stored at high temperature. Shen et al further teach that a composition in a dried state is useful in shipping and storage of commercial preparations for use in e.g., nucleic acid amplification kits (page 6, lines 39-41). Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have been motivated to provide the labeling composition as taught by Godiska et al in a dried state for the advantage taught by Shen et al that a nucleic acid composition present in a dried state is useful in shipping and storage of commercial preparations due its increase stability.

Regarding claim 5, Godiska et al teach a method of making a labeled probe for a nucleic acid template, wherein the method comprises the steps of providing a nucleic acid template and a labeling composition and incubating the nucleic acid template under chain extension conditions with the labeling composition to produce a labeled probe (col. 8, lines 27-31).

5. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Godiska et al. in view of Shen et al. and further in view of Hoeltke et al. (5,814,502, effective filing date October 1994). Regarding claim 6, Godiska et al in view of Shen et al teach a labeling composition and method of making a labeled probe comprising a number of method steps wherein the labeled compositions comprises a random mixture of oligonucleotides which are 6-mers and said composition present in

a dry state. The labeling composition of the disclosure differs from that of the references in that the references do not expressly teach the concentration of the random mixture of oligonucleotides. However the optimal contents range would have been determined by the practitioner based on desired properties of the random oligonucleotides, desired lengths of the random oligonucleotides and desired results. For example, in a method for labeling nucleic acid, Hoeltke et al teach a random mixture of oligonucleotides wherein the concentration range of approximately 15 to 80 OD/ml is selected for the various random primers which are 6-mers to 15- mers. Hoeltke et al further teach that depending on the primer length, the optimal contents range will change (col. 2, lines 55-60 and col. 3, lines 38-42). Therefore, in view of the foregoing, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the concentration range of the random mixture of oligonucleotides is variable based the practitioner's preference as well as the length of the primers as suggested by Hoeltke et al.

Applicant's traversal

6. Applicant traverses the rejection on the following grounds: Applicant states that the rejection should be withdrawn because the selection of 6-mers to 8-mers does constitute a critical range (see application examples and the art fails to suggest that short primers (6-8 mers) would be desirable in a dried primer system. Applicant states that the Applicant's examples demonstrate a critical difference in self-priming activity and labeling intensity between 6-8 mers and 9-mers. Applicant contends that more specifically, there is noting in Godiska that teaches that the selection

of 6-mers to -8 mers constitutes a critical range and that short primers (6-8 mers) would be desirable in a dried primer system. Applicant contends that while Godiska discloses a random mixture of 6-mers and other ingredients, the Examiner acknowledges that Godiska does not teach a labeling composition in a dried state. Applicant states that moreover, there is nothing in Godiska that teaches that a selection of 6-mers to 8-mers is important in either the liquid or freeze dried state to reduce self-annealing. Applicant argues that in fact, self annealing is not mention at all. Applicant further argues that in addition, Shen which discloses 48-mer and 22-mer primers fail to suggest that dried primers should be shortened or alternatively any reason why the primers of Godiska should be dried. Applicant states that this is because the prior art generally taught that longer primers were preferred because longer primers have higher melting temperatures and are thus more specific. Applicant contends that moreover, Shen acknowledges that "whether a particular composition will function to preserve biological activity for a particular biologically active material is not a *priori* predictable" and only discloses freeze-drying and an "option" and in addition, Shen fails to provide any reason why the primer of Godiska should be dried given the fact that shorter primers were thought to be inherently more stable and there was no reasons to believe that the shorter Godiska primers would benefit from being in the freeze dried kit.

Finally, Applicant concludes that Hoeltke does nothing to make up for the deficiencies of Godiska and Shen with respect to teaching the subject matter of independent claim 1. Applicant states that while it teaches that optimum detergent concentrations vary for different primer lengths

it does not tech that 6-8 mers would be preferred to longer oligonucleotides in a dried reagent system. Applicant states that for these reasons, the rejection should be withdrawn.

Examiner's Response

7. Applicant's arguments filed in Paper No. 27 have been fully considered but they are not persuasive. Firstly, in response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, as noted in the prior Office action, the prior art (Godiska et al) teaches a labeling composition comprising a random mixture of oligonucleotides that are 6-mers. Godiska et al. further teach wherein the composition further contains at least a supply of nucleotide for chain extension, a labeled nucleotide, and a polymerase enzyme. The reference does not teach the labeling composition in a dried state. This limitation however is found in the secondary reference of Shen. Shen teaches a composition comprising primers, a polymerase enzyme, a supply of nucleotides for chain extension and a stabilizer which are all present in a dried state. Shen provides motivation for wanting a composition in a dried state in the teaching that "a composition in a dried state is advantageous because the composition is stable for a prolonged period, even when stored at high temperatures". The reference provides further motivation in the teaching that a composition in a dried state is useful in shipping and storage of commercial preparations for use in e.g., nucleic acid amplification.

With respect to claim 6, the reference of Godiska in view of Shen teaches a labeling composition and a method of making a labeled probe wherein the labeled compositions. The references do not teach the concentration of the random mixture of oligonucleotides. However, this deficiency is demonstrated by Hoeltke et al. which supports the Examiner's position that the optimal content range would have been determined by the practitioner based on the desired properties of random oligonucleotides, desired lengths of the random oligonucleotides and desired results. Hoeltke et al. demonstrates the variably in the optimal content range of primers 6-15 mers in length.

In response to Applicant's argument that the prior art fails to show teaching of the selection of 6-mers to 8-mers (a critical range) as desirable in a dried primer system, it is noted that the claims as written broadly encompasses a random mixture of oligonucleotides that are 6-mers **or** a random mixture of oligonucleotide that are 7-mers **or** a random mixture of oligonucleotides that are 8-mers **or** a combination therein. This limitations is provided by the primary reference of Godiska who teaches random 6-mers. Furthermore, the courts have established in *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955) that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation". The court has established that "a claim which falls within the broad scope of the references is held unpatentable thereover because, among other reasons, there is no evidence of the **criticality** of the claimed ranges" (See *in re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA)). Therefore, to reiterate, the random mixture of oligonucleotides (6-mer to 8-mer) of the claimed invention falls *within* the range of the random mixture of oligonucleotides (6-mers) of Godiska. The arguments are

not sufficient to overcome the prior art rejection. Accordingly, the rejections under 35 U.S.C. 103(a) are maintained.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Cynthia Wilder whose telephone number is (703) 305-1680. The Examiner can normally be reached on Monday through Thursday from 9:30 am to 6:30 pm and on Friday from 9:30 am to 1:30 pm.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (703) 308-1119. The official fax phone number for the Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Group's receptionist at (703) 308-0196.

cbw
August 5, 2003

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

8/6/03